Southall And Brent REvisited: Cohort profile of SABRE, a UK population-based comparison of cardiovascular disease and diabetes in people of European, Indian Asian and African Caribbean origins

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COHORT PROFILE

Southall And Brent REvisited: Cohort profile of SABRE, a UK population-based comparison of cardiovascular disease and diabetes in people of European, Indian Asian and African Caribbean origins

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How did the study come about?

The Baseline Southall and Brent Studies (1988–91)

Comparisons of chronic disease in migrant and host populations have provided valuable aetiological insights, and furthered the understanding of balance between genetic and environmental influences on the disease. The UK is home to several migrant groups, the largest and longest established being of Indian Asian and African Caribbean origins. One of the earliest and largest waves of Indian Asian migration to the UK followed the 1947 partition of India. As these migrants reached middle age in the 1970s, it became increasingly apparent, both in the UK and elsewhere overseas, that this population was at greatly increased risk of cardiovascular disease (CVD), both coronary heart disease (CHD) and stroke, compared with host populations.[1–6] Initial exploration of conventional risk factors, such as diet, total cholesterol, smoking and blood pressure, showed that these differed markedly between ethnic subgroups and were often more favourable than the host UK population, and therefore these factors could not account for the excess CVD risk observed in all Indian Asian subgroups (such as Indians of Gujarati/Hindu Punjabi/Sikh Punjabi origin, Pakistanis and Bangladeshis). Notably, a greater prevalence of diabetes was found in all Indian Asian subgroups, which linked with the observation of greater fasting hyperinsulinaemia, led us to hypothesize that insulin resistance, associated with upper body fat distribution, could underpin the excess diabetes, hypertriglyceridaemia and CHD in Indian Asians.[3] This hypothesis was tested in the Southall study, a large population-based inter-ethnic cross-sectional study of middle-aged men and women carried out between 1988 and 1990.[7]

A large number of migrants of Black African descent from the Caribbean and West Africa also arrived in the UK during the post–Second World War period, encouraged by the UK government in an effort to fill the many vacancies for key workers.[8] As these African Caribbean migrants were also reaching middle age in the 1980s, an intriguing paradox was emerging in the UK, which had been noted previously in similar populations in the USA and Caribbean. Despite high rates of diabetes, people of African and African Caribbean descent had relatively low CHD risks compared with White European ethnic origin populations.[6,9–11] In stark contrast, stroke-related mortality was doubled and mortality from hypertensive disease was increased between 4-fold (men) and 7-fold (women) in Caribbean-born migrants compared with the general UK population.[10] The latter finding was especially puzzling, as previous population-based studies did not provide unequivocal evidence that blood pressure or the prevalence of hypertension were elevated in people of Black

African descent.[12–14] Exploration of the diabetes/CHD paradox and definitive exploration of ethnic differences in resting and ambulatory blood pressure formed the basis of the Brent population-based comparison of African Caribbean and European middle-aged men and women.[15]

This cross-sectional comparison followed the successful completion of the Southall study in 1990. The Southall and Brent studies were performed according to identical protocols by the same team, using the same equipments and hospital laboratories. The geographical areas of the baseline studies are contiguous and the two studies were conducted consecutively. In order to improve statistical power, the two baseline data sets have now been amalgamated. Together, the Southall and Brent studies form the basis of the largest UK population-based tri-ethnic cohort.

Southall And Brent REvisited (2008–13)

Cross-sectional analysis of the Southall and Brent studies yielded important information on disease prevalence and associations (see below), but could only hint at causality. In addition, first-generation migrants as a cohort are now reaching pensionable age, where disease burden is anticipated to be high, yet little data exist for this age group. In particular, heart failure, as a consequence of CHD, diabetes and hypertension, a rarity in middle-aged individuals, now becomes especially prevalent, causing more than one-third of all deaths in older age.[16] Finally, interim mortality follow-up analyses of this cohort showed striking ethnic differences in the effects of dysglycaemia on CVD mortality (see What Has It Found? section), adding urgency to the need for follow-up study of cardiometabolic health and the mechanisms underlying ethnic differences.

The Southall And Brent REvisited (SABRE) study was initiated in 2008 as a 20-year follow-up of the two baseline studies.

Ethics committee approval was obtained for both baseline studies as well as for SABRE.

What does the study cover and how has this changed?

Broadly, the baseline studies were set up to examine, in cross section, the associations between components of the insulin resistance or 'metabolic' syndrome in each of the three ethnic groups and to determine how these associations might underlie the higher rates of CHD in Indian Asians and the higher rates of hypertensive target organ damage and stroke in African Caribbeans.

The SABRE follow-up study (2008–13) continues to focus on ethnic differences in cardiometabolic risk. We are quantifying cardiometabolic events during the follow-up period in both surviving and deceased participants using questionnaires to participants and primary-care record review, and in survivors, by measuring subclinical CVD. We will address the following primary research questions:

- Is the greater risk of CHD in Indian Asians explained by a hyperglycaemia-associated adverse lipid and lipoprotein profile compared with Europeans?
- Is the greater risk of stroke and magnetic resonance imaging (MRI)-detected subclinical cerebral infarct in African Caribbeans explained by hyperglycaemia-associated loss of nocturnal blood pressure dipping compared with Europeans?
- Does subclinical circulatory disease differ by ethnicity, and if so, is this predicted and explained by differences in expression of the cardiometabolic syndrome?
- Do current thresholds for risk-factor interventions need modifying for UK ethnic minority groups?

Who is in the sample?

The Southall study (1988–90) was the first of the two baseline studies.[7] A target sample of 3000 men aged 40–69 years of Indian Asian and European descent was chosen to have 90% power to detect at 5% significance a relative risk of 1.5 for prevalent CHD in Indian Asian compared with European men. The sample was assembled from two sources selected for the ethnic mix of the potential participants: industrial workforces and general practitioners' (GPs') lists. The general practice component was supplemented with a target sample of 600 women and was drawn from 16 general practices in the Southall and Greenford areas of west London. A small number of African Caribbean participants (223) who appeared in this sampling frame were also included. For the industrial sample, four factories in West London were chosen on the basis of the ethnic mix of their workforces. The overall response rate for the Southall study was 64% for Indian Asian men (1421 out of 2230) and 67% in non-Asian men (1772 out of 2660) (Table 1).

In the Brent Study (1990–91),[15] the target sample was based on the lists of six general practices. A sample of 300 participants in each sex and ethnic group (European and African Caribbean) aged 40–69 years was calculated to have 90% power to detect a difference of 3% in mean systolic and diastolic blood pressures at a 5% level of significance. With the help of practice staff, potential participants were assigned to one of the five ethnic groups: European, South Asian, African Caribbean, other and unknown. The relative proportions of these groups varied by general practice, although the proportion of participants of unknown ethnicity was small. A random sample from the combined African Caribbean and unknown group, stratified by 5-year age group and sex, was selected, and an equal

Table 1 Summary of Southall and Brent study recruitment (1988–91) and response rates and survival to SABRE follow-up (commencing 2008)

	Delivered invitations	Agreed, *n* (%)	Ethnicity			Survivors (as on 1 July 2008)	
Southall				M	F		
Workplace	1141	808 (71%)	E:	1516	246	E:	1430 (81%)
			IA:	1420	291	SA:	1466 (86%)
General practice	4713	2946 (63%)	AC	209	14	AC:	193 (87%)
			Other:	59			
Brent							
General practice	2088	1218 (58%)	E:	272	313	E:	513 (88%)
			AC:	244	334	AC:	525 (91%)
			Other:	55			
Southall and Brent							
Combined studies	7942	4972 (63%)	E:	1787	559	E:	1943 (83%)
			IA:	1420	291	SA:	1466 (86%)
			AC:	453	348	AC:	718 (90%)
			Other:	114			

E: European; IA: Indian Asian; AC: African Caribbean.

sample of Europeans was chosen in the same manner. The response rate was 58% (Table 1). Although it was not possible to assign ethnicity to all potential participants invited, the response rates were similar in the two ethnic groups in those participants in whom ethnicity could be assigned.

All South Asian and African Caribbean participants are first-generation migrants to the UK.

How often have they been followed up?

Since the baseline studies, participants have been flagged for mortality by the Office for National Statistics and analyses of death certificate data have been performed. A pilot postal follow-up in 176 people randomly selected from both baseline studies was conducted in 2004. This feasibility assessment informed the grant application for follow-up of the entire study population. The current study (SABRE) is the first follow-up of survivors.

What has been measured?

At baseline, participants were invited to attend clinics in local hospitals and health centres for a health check after an overnight fast. Prior to the examination, participants were asked to complete a self-administered questionnaire that included items on past medical history (including diabetes and the Rose angina questionnaire,[17] medication, smoking, alcohol intake, physical activity, dietary information and occupation, together with questions regarding current and childhood socio-economic circumstances. Ethnicity was described by the interviewer based on appearance and parental origin. Clinical measurements were performed to a standard protocol and are listed in Table 2. Baseline characteristics are detailed in Table 3.

In addition to the above, Brent study participants were invited to take part in substudies including echocardiography, retinal photography and 24-h ambulatory blood pressure monitoring (Table 2).

In the SABRE follow-up, all participants currently living in England or Wales are invited by letter to attend the study clinic at St Mary's Hospital London following an overnight fast. Taxi transport is provided for local participants and travel costs are reimbursed for those who live outside the London area. Participants are asked to complete a detailed questionnaire regarding medical history, lifestyle and socio-economic circumstances. They then undergo a series of comprehensive clinical measurements as detailed in Table 2.

We offer home visits by a trained nurse for those who live locally but who are unable or unwilling to attend the clinic. These home visits include anthropometric and blood pressure measurements, plus urine and fasting blood samples. As part of the informed consent procedure, participants can also choose to limit their participation to completion of the questionnaire and/or consent for medical record review.

Cardiovascular and diabetes-related events that have occurred since the baseline studies are identified from primary-care medical record review and from

Table 2 Southall and Brent baseline studies and SABRE follow-up measurements

Investigations/measurements	Baseline studies (1988–91)	SABRE study follow-up (2008–12)
Age of participants, years	40–69	57–90
Anthropometrics		
Circumferences: waist, hip, thigh	✓	✓
Sagittal diameter	✓	–
Truncal and peripheral skinfold thicknesses	✓	–
Height	✓	✓
Leg length	–	✓
Weight	✓	✓
Body fat		
Bioimpedance		
Percent body fat	–	✓
Fat mass	–	✓
CT (for fat distribution)		
Thigh (single slice, mid-thigh)	–	✓
Abdomen (single slice L4)	–	✓
Bloods		
Fasting		
Glucose, insulin	✓	✓
$HbA1_c$	–	✓
Total cholesterol, triglycerides, HDL cholesterol	✓	✓
Serum creatinine	–	✓
Liver function tests	–	✓
Lipoprotein subfractions (NMR spectroscopy)	–	✓
Apolipoprotein a/b	✓ (subset)	✓
APOE genotype	✓ (subset)	✓
Inflammatory markers (TNFα, CRP, IL-6, NT ProBNP, PAI 1)	✓	✓
Stored blood for future analyses	✓	✓
Two-hour post-glucose challenge (if not known to have diabetes)		
Glucose, insulin	✓	✓
Total cholesterol, triglycerides, HDL cholesterol	✓	–
Urine		
Timed overnight urine collection for albumin excretion rate	✓ (subset)	–
Albumin creatinine ratio	✓	✓
Blood pressure		
Resting		
Brachial sitting	✓	✓
Brachial lying	–	✓
Ankle lying	–	✓
24-hour ambulatory blood pressure	✓ (subset in Brent only)	✓
ECG (resting, 12 lead)	✓	✓
Echocardiography and vascular measurements		
2D echocardiography	✓ (subset in Brent only)	✓
Left ventricular function, wall thickness, cavity dimensions, Speckle tracking (ventricular dyssynchrony tissue velocity, strain and rotation)	–	✓
Tissue Doppler imaging		
Tissue velocities	–	✓
3Dk echocardiography		
Left ventricular volumes, wall masses, cavity dimensions, ventricular function and ventricular dyssynchrony	–	✓
Left ventricular remodelling index	–	✓
Vascular		
Carotid intima media thickness	–	✓
Pulse wave velocity (carotid-femoral)	–	✓
Wave intensity analysis	–	✓
Coronary artery calcification (CT)	–	✓
Cerebral MRI		
White matter lesions, sulcal and ventricular grades	–	✓
Non-haemorrhagic infarcts and haemorrhagic lesions	–	✓
Hippocampal volumes	–	✓
Cognitive function testing		
Participant tests, plus key informant perspective	–	✓
Eye photography		
Retinal photography (four-field, both eyes)(analysis for retinal vascular architecture, age-related macular degeneration and diabetic retinopathy)	✓ (subset in Brent)	✓
Lens photography (opacities and cataracts)	–	✓
Visual acuity	–	✓
Medical history		
Participant recall	✓	✓
Primary-care medical record review	–	✓
Lifestyle/behaviours	✓	✓
Smoking, alcohol consumption, physical activity	✓	✓
Diet	✓	–
Socio-economic circumstances		
Childhood	✓	–
Current	✓	
Quality of life (EQ5D)	–	✓
Activities of daily living	–	✓
Family history of diabetes/ heart disease	–	✓

participant questionnaire responses. Medical record review is undertaken by trained members of the research team in local general practices and at primary care trusts where the records of deceased participants are stored. In the cases where participants have moved outside the local area, their GP is asked to complete the same case report form.

Reminder letters are sent to non-responders after 2 weeks. If there is no response after a reminder, then trained interviewers from the National Centre for Social Research (NatCen) carry out home visits in the north-west London area, with the aim of recruiting participants for full clinical follow-up and/or completion of the questionnaire and/or consent for medical record review.

What is attrition like?

As SABRE represents the first individual follow-up of surviving participants and is in the mid-recruitment phase, data on attrition are limited. We used the NHS tracing system to trace the cohort in 2008. Currently, we are nearly 2 years into the follow-up study and have approached 2925 of 4127 surviving participants. We have identified 431 people who either do not have a valid contact address or who were away when we attempted to contact them. This represents 8% of Europeans, 11% of Indian Asians and 19% of African Caribbeans. Although 22% of survivors (38% of Europeans, 7% of Indian Asians and 8% of African Caribbeans) have moved to areas outside north-west London, the majority of dispersion is to other areas of greater London or the surrounding counties within a 80 km radius.

In the feasibility study of 176 people, non-responders ($n = 60$) tended to have worse baseline risk factor profiles than responders, although the differences were seldom significant and not consistently in one direction. Based on the feasibility study, we expect overall response rates to be 70, 65 and 60% among European, Indian Asians and African Caribbeans, respectively. After nearly 2 years into the follow-up study, among 2925 approached, 61% of Europeans, 56% of Indian Asians and 52% of African Caribbeans have agreed to participate. We expect these rates to be substantially boosted following a further attempt to revisit or trace those who were initially away or whose addresses were unknown, and most importantly, following home visits by NatCen interviewers in the north-west London area.

At the expected response rates (70, 65, 60%), SABRE will have $\geqslant$80% power at 5% significance to examine the effects of major risk factors for CHD and stroke separately and to examine the different magnitudes of effect of diabetes [detectable hazard ratios in whole study population: new CHD events (fatal and non-fatal): Indian Asians vs Europeans: 1.4, African Caribbeans vs Europeans: 0.6, and for new stroke events (fatal and non-fatal): Indian Asians vs Europeans: 1.7, African Caribbeans vs Europeans: 2.0].

What has it found?

The baseline Southall study was the first to report the high prevalence of the insulin resistance or cardiometabolic syndrome in association with a striking tendency to central obesity in British Indian Asian migrants—these findings were common to diverse South Asian subgroups such as Hindus, Sikhs and Muslims. These findings led us to suggest that insulin resistance might be the underlying cause of the increased susceptibility to CHD and stroke among Indian Asians.[7,18] The Brent study, on the other hand, reported that while African Caribbeans were as dysglycaemic, they were less hyperinsulinaemic than Indian Asians. They were not centrally obese and had favourable blood lipid profiles, suggesting that the causes of diabetes in African Caribbeans may be different from those in Indian Asians and this might also explain why CHD mortality in African Caribbeans is low, despite the high prevalence of diabetes and hypertension.[19] In addition, resting and ambulatory blood pressure recordings in a subgroup of Europeans and African Caribbeans ($n = 319$) demonstrated that the higher resting blood pressures in African Caribbean women may be enough to explain their excess stroke mortality, but that blood pressure did not explain the excess stroke rates in African Caribbean men. Smaller declines in nocturnal blood pressure may further contribute to the excess of hypertensive target organ damage in African Caribbeans.[15] Echocardiographic study demonstrated that African Caribbeans had greater left ventricular structural impairment than Europeans, and that remodelling patterns of the left ventricle in response to hypertension differed, with greater wall thickening and cavity narrowing compared with Europeans.[20] This pattern of remodelling in other studies is found to have more adverse implications for downstream mortality than patterns more commonly observed in people of European origin.

Analyses of cardiovascular mortality during the first 16 years of follow-up suggested that diabetes [defined retrospectively by World Health Organisation (WHO) 1999 criteria[21]] exerts a remarkably 'toxic' effect with regard to both CHD and stroke mortality in people of Indian Asian origin.[22] In people of African Caribbean origin, diabetes 'toxicity' was particularly striking in association with stroke mortality. At 16 years of follow-up, African Caribbeans with diabetes were six times more likely to die from stroke compared with Europeans [incidence rate ratio adjusted for age, systolic blood pressure and smoking status: 6.7 (95% confidence interval 1.4–32.5, $P = 0.018$)].[23] Further unpublished analyses demonstrated similar effects on mortality in both Indian Asians and African Caribbeans in association with

Table 3 Baseline characteristics (1988–91) in the combined Southall and Brent study population

	Means ± SD, medians (25th, 75th percentiles)				
	European men	Indian Asian men	*P*-value (IA vs E)	African Caribbean men	*P*-value (AC vs E)
Men					
Number	1787	1420		453	
Age	52.7 ± 7.1	50.7 ± 7.0	<0.001	53.5 ± 5.8	0.035
Height, cm	174.2 ± 6.9	169.8 ± 6.5	<0.001	171.9 ± 6.7	<0.001
Weight, kg	79.6 ± 12.9	74.5 ± 11.0	<0.001	74.5 ± 10.3	0.010
Waist circumference, cm	91.9 ± 11.0	92.9 ± 9.6	0.013	89.4 ± 9.8	<0.001
Hip circumference, cm	97.3 ± 6.7	94.6 ± 6.2	<0.001	94.9 ± 6.4	<0.001
Waist-to-hip ratio	0.94 ± 0.07	0.98 ± 0.06	<0.001	0.94 ± 0.06	0.66
Body mass index, kg/m^2	26.2 ± 3.9	25.8 ± 3.3	0.052	26.3 ± 3.3	0.24
Systolic blood pressure, mmHg	121 (112, 133)	123 (113, 136)	<0.001	126 (116, 137)	<0.001
Diastolic blood pressure, mmHg	77 (70, 84)	80 (74, 87)	<0.001	80 (73, 89)	<0.001
Treated hypertension	150 (8%)	190 (13%)	<0.001	85 (19%)	<0.001
Prior CHD	169 (9%)	130 (9%)	0.79	23 (5%)	0.003
Prior stroke	19 (1%)	25 (2%)	0.088	12 (3%)	0.009
Known diabetes	55 (3%)	185 (13%)	<0.001	46 (10%)	<0.001
Diabetes by WHO 1999 criteria, *n* (%)[b]	127 (7%)	311 (22%)	<0.001	83 (18%)	<0.001
Impaired fasting glucose (IFG) (isolated)[b]	171 (10%)	121 (9%)	0.31	52 (12%)	0.21
Impaired glucose tolerance (IGT) (isolated or both IFG and IGT)[b]	50 (3%)	70 (5%)	0.002	44 (10%)	<0.001
Fasting glucose, mmol/l	5.4 (5.1, 5.8)	5.5 (5.1, 6.0)	<0.001	5.6 (5.2, 6.1)	<0.001
Fasting insulin, pmol/l	51.4 (34.0, 75.0)	75.0 (50.7, 110.4)	<0.001	59.0 (39.5, 86.3)	<0.001
Two-hour post-glucose load glucose, mmol/l	5.0 (4.2, 5.9)	5.5 (4.6, 6.6)	<0.001	5.8 (5.0, 7.1)	<0.001
Two-hour post-glucose load insulin, pmol/l	136.8 (80.6, 238.9)	283.4 (163.9, 517.4)	<0.001	155.6 (104.2, 250.0)	0.02
HOMA insulin resistance	1.8 (1.1, 2.7)	2.6 (1.7, 3.9)	<0.001	2.1 (1.3, 3.1)	0.003
Total cholesterol	5.8 (5.1, 6.6)	5.7 (5.0, 6.4)	<0.001	5.4 (4.7, 6.2)	<0.001
Fasting triglycerides, mmol/l	1.4 (1.0, 2.0)	1.6 (1.1, 2.3)	<0.001	1.0 (0.8, 1.5)	<0.001
HDL cholesterol, mmol/l	1.3 (1.0, 1.5)	1.2 (1.0, 1.4)	<0.001	1.4 (1.2, 1.7)	<0.001
Microalbuminuria, *n*/total number with overnight urine collection[a] (%)	64/1055 (6%)	44/763 (6%)	0.79	20/288 (7%)	0.59
Urine AER	4.0 (2.9, 6.1)	3.5 (2.5, 6.2)	<0.001	5.4 (3.6, 8.9)	<0.001
Smoking status, % never/ex/current	29/40/32	74/11/15	<0.001	54/19/26	<0.001
Physical activity score MJ/week	3.9 (1.2, 5.1)	3.5 (1, 4)	<0.001	3.7 (1.2, 5.8)	0.010
Women					
Number	559	291		348	
Age	52.9 ± 6.7	50.7 ± 6.8	<0.001	52.9 ± 6.0	0.94
Height, cm	161.1 ± 6.4	154.7 ± 6.4	<0.001	160.9 ± 5.5	0.77
Weight, kg	67.6 ± 13.2	65.2 ± 10.7	0.005	76.1 ± 13.4	<0.001
Waist circumference, cm	80.0 ± 12.2	85.8 ± 11.0	<0.001	88.7 ± 11.4	<0.001
Hip circumference, cm	99.0 ± 8.7	98.3 ± 8.1	0.26	102.8 ± 9.1	<0.001
Waist-to-hip ratio	0.81 ± 0.08	0.87 ± 0.09	<0.001	0.86 ± 0.08	<0.001
Body mass index, kg/m^2	26.1 ± 4.8	27.3 ± 4.6	<0.001	29.4 ± 4.8	<0.001
Systolic blood pressure, mmHg	118 (108, 128)	123 (109, 136)	<0.001	130 (119, 142)	<0.001
Diastolic blood pressure, mmHg	75 (68, 81)	76 (70, 83)	<0.001	81 (73, 89)	<0.001
Treated hypertension	59 (11%)	38 (13%)	0.28	102 (29%)	<0.001

(continued)

Table 3 Continued

	Means ± SD, medians (25th, 75th percentiles)				
	European women	Indian Asian women	*P*-value (IA vs E)	African Caribbean women	*P*-value (AC vs E)
Prior CHD	32 (6%)	4 (1%)	0.003	17 (5%)	0.59
Prior stroke	7 (1%)	3 (1%)	0.78	6 (2%)	0.56
Known diabetes	13 (2%)	27 (9%)	<0.001	39 (11%)	<0.001
Diabetes by WHO 1999 criteria[b]	24 (4%)	44 (15%)	<0.001	68 (20%)	<0.001
IFG (isolated)[b]	36 (6%)	3 (1%)	<0.001	18 (5%)	0.44
IGT (isolated or both IFG and IGT)[b]	34 (6%)	20 (7%)	0.64	47 (14%)	<0.001
Fasting glucose, mmol/l	5.3 (4.9, 5.7)	5.1 (4.8, 5.6)	0.005	5.6 (5.1, 6.2)	<0.001
Fasting insulin, pmol/l	36.8 (25.6, 56.0)	53.1 (37.5, 80.6)	<0.001	64.4 (41.6, 90.3)	<0.001
Two-hour post-glucose load glucose, mmol/l	5.7 (5.0, 6.6)	5.7 (94.9)	0.52	6.6 (5.7, 7.8)	<0.001
Two-hour post-glucose load insulin, pmol/l	148.3 (97.2, 226.8)	309.7 (185.4, 526.4)	<0.001	255.2 (175.4, 388.2)	0.002
HOMA insulin resistance	1.3 (0.8, 2.0)	1.7 (1.2, 2.9)	<0.001	2.4 (1.5, 3.4)	<0.001
Total cholesterol, mmol/l	6.0 (5.2, 6.9)	5.7 (5.0, 6.4)	<0.001	5.6 (4.8, 6.5)	<0.001
Fasting triglycerides, mmol/l	1.2 (0.9, 1.7)	1.4 (1.1, 1.9)	<0.001	1.1 (0.8, 1.4)	<0.001
HDL cholesterol, mmol/l	1.6 (1.3, 1.9)	1.4 (1.2, 1.6)	<0.001	1.6 (1.4, 1.9)	0.20
Microalbuminuria, *n*/total number with overnight urine collection[a] (%)	12/433 (3%)	6/200 (3%)	0.88	22/254 (8%)	0.001
Urine AER	3.1 (2.2, 4.4)	3.1 (2.0, 5.0)	0.96	4.7 (3.2, 8.0)	<0.001
Smoking status, % never, ex, current					
Physical activity score MJ/week	3.8 (1.2, 5.1)	1.5 (1.0, 3.5)	<0.001	3.7 (1.2, 5.8)	0.52

AER: albumin excretion rate; HOMA: homeostasis model assessment.
[a]Overnight urine collection not complete for whole study population.
[b]WHO 1999 criteria applied retrospectively.

fasting and post-challenge glucose in both univariate and multivariate analyses (unpublished data, Figure 1). These interactions between ethnicity and dysglycaemia could not be explained by conventional risk factors (refs[22,23] and unpublished data) and were evident even in those whose diabetes had not been diagnosed before the first baseline study visit (Figure 1). However, numbers of deaths at this stage of follow-up were small, and it is apparent that there is an urgent need to assess non-fatal events and subclinical CVD in association with dysglycaemia in our surviving cohort.

What are the main strengths and weaknesses?

This is the largest tri-ethnic UK cohort and now has a 20-year follow-up. The South Asian and African Caribbean participants form a unique group of British first-generation migrants—a precious resource. The baseline studies were performed to a strict protocol and have resulted in detailed phenotyping of the group in middle age. The participants are now of an age to be at maximal risk of cardiovascular events, and current follow-up involves extensive cardiovascular assessment using state-of-the-art techniques. Particular strengths lie in the range and detail of the follow-up measurements of subclinical disease. These include indicators of suboptimal heart function and structure. Added value will be gained from validation of 2D echocardiographic measurements against gold standard 3D techniques for assessment of cardiac volumes. Cognitive function and MRI assessment of subclinical cerebral changes will provide unique data in this older population. Quantification of body-fat distribution using computed tomography (CT) together with glucose tolerance testing and measurements of lipoprotein subfractions will inform understanding of the mechanisms underlying the marked ethnic differences in the manifestations of insulin resistance. Studies involving ethnic group comparisons not only increase understanding of genetic and lifestyle effects on disease risk but also form important natural experiments where the marked ethnic differentials in clustering of risk factors enable elucidation of the relative roles of each in disease causation. Finally, using baseline

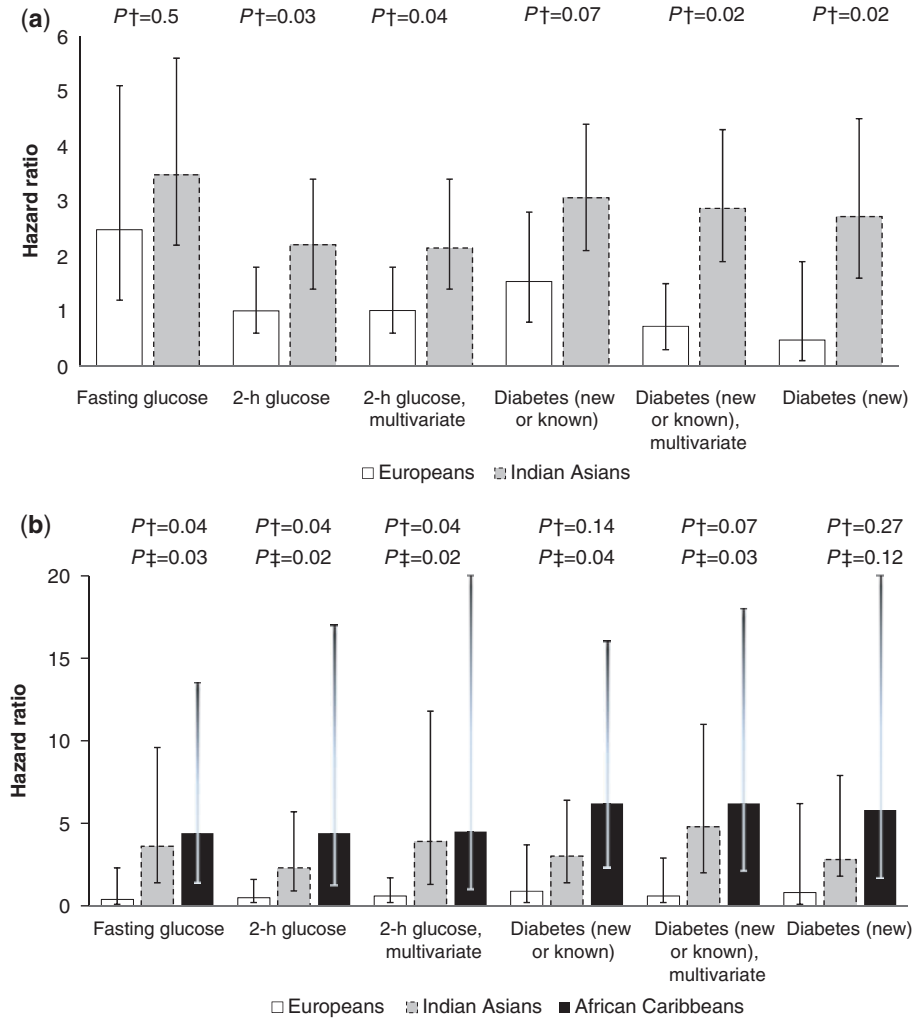

Figure 1 Southall and Brent studies mortality follow-up to 2007. (a) Age-adjusted univariate and multivariate Cox regression analysis of associations of measured risk factors with CHD mortality in Europeans and Indian Asians. (b) Age-adjusted univariate and multivariate Cox regression analysis of associations of measured risk factors with stroke mortality in Europeans, Indian Asians and African Caribbeans. Multivariate models adjusted for triglyceride, waist circumference, insulin, cholesterol, blood pressure and smoking. $P^{\dagger}$ = interaction *P*-value: Indian Asians vs Europeans. $P^{\ddagger}$ = interaction *P*-value: African Caribbeans vs Europeans. Diabetes defined according to WHO criteria, 1999[21]

risk factor associations with fatal and non-fatal events, SABRE will uniquely be able to inform ethnicity-specific thresholds for CVD risk factor intervention in the UK.

The weaknesses of the study lie mainly in the single follow-up at 20 years and in loss to follow-up. However, we are conducting review of medical records together with participant recall of major cardiovascular events since the baseline studies. This complementary approach has been shown to provide a valid method of identifying morbid events during lengthy follow-up periods.[24] In addition, we have full mortality follow-up since the baseline follow-up, and review of medical records will complement death certificate information for deceased participants. Loss to clinical follow-up is likely to be substantial, particularly in older migrant populations, as retirement often involves a return to the home country for protracted periods. However, our pilot study data and initial responses indicate that most European and Indian Asian participants are traceable to a UK address and are willing to take part in the follow-up study. It is our experience that African Caribbeans tend to favour face-to-face contact over a postal approach for recruitment; hence intensive efforts will be made to trace and visit African Caribbean non-responders.

Can I get hold of the data? Where can I find out more?

Data will be stored by the UK Data Archive from 2014. We welcome proposals from 2014 onwards for collaborative study of baseline and follow-up data. Please contact Professor Nish Chaturvedi (n.chaturvedi@

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Appendix 1

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